

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

REC'D 21 JUN 2001

WIPO

PCT

Applicant's or agent's file reference 98-75PC		<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/00396	International filing date (day/month/year) 07/01/2000	Priority date (day/month/year) 07/01/1999	EPO - DG 1
International Patent Classification (IPC) or national classification and IPC C12N15/11		22. 10. 2001	
Applicant ZYMOGENETICS, INC.		(40)	

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.


2. This REPORT consists of a total of 5 sheets, including this cover sheet.

- ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 27/07/2000	Date of completion of this report 19.06.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized officer Masturzo, P Telephone No. +31 70 340 2275



22/10/2001

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US00/00396

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, pages:**

1-117 as originally filed

**Claims, No.:**

1-55 as originally filed

56-62 as received on 16/01/2001 with letter of 16/01/2001

**Drawings, sheets:**

1/14-14/14 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

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- ☐ the description, pages:  
☒ the claims, Nos.: 59  
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.  
☒ claims Nos. 1-56.

because:

- ☒ the said international application, or the said claims Nos. 1-56 relate to the following subject matter which does not require an international preliminary examination (*specify*):  
**see separate sheet**
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.  
☐ the computer readable form has not been furnished or does not comply with the standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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## 1. Statement

Novelty (N)	Yes:	Claims	58-60
	No:	Claims	57,61-62
Inventive step (IS)	Yes:	Claims	58-60
	No:	Claims	57,61-62
Industrial applicability (IA)	Yes:	Claims	57-62
	No:	Claims	1-56

2. Citations and explanations  
**see separate sheet****VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:  
**see separate sheet**

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**EXAMINATION REPORT - SEPARATE SHEET**

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Reference is made to the following documents:

D1: WO-A-39361 (St. Jude Hospital)

D2: Science 278, pages 138-141.

Ref. Point III

Claims 1-56 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Ref. Point V.

D1 discloses (see sequences on pages 69ff). sequences comprising those of claims 56-57 and 61-62, and obtained in a pertinent way. Therefore these claims are objected to under Art. 33(2) PCT as they are not new. In fact "comprising" does not mean "limited to", which wording would have guaranteed the recognition of novelty.

The best state of art are D1 and D2. They disclose a soluble TNF receptor named TAC1.

The objective problem underlying the application is the provision of alternative soluble receptors for TNF. The applicant has provided a soluble receptor for TNF named BR43x2 and has provided evidence that it can be used for pertinent purposes, essentially with therapy of autoimmune diseases.

These reasons witness in favor of a recognition of an inventive step for claims 1-55 and 58-60 under Art. 33(3) PCT.

Ref. Point VIII

Claim 59 has been suppressed, therefore no objection under Art. 6 and Rule 6 PCT subsists.

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WO 00/40716

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Substitute Sheet  
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(40)

56. An isolated polynucleotide molecule encoding a polypeptide of SEQ ID NO:2.

57. An isolated polynucleotide molecule of SEQ ID NO:1.

58. An expression vector comprising the following operably linked elements:

- a transcription promoter;
- a polynucleotide molecule according to claim 56; and
- a transcription terminator.

59. A cultured cell into which has been introduced an expression vector according to claim 58, wherein said cultured cell expresses said polypeptide encoded by said polynucleotide segment.

60. A method of producing a polypeptide comprising:  
culturing a cell into which has been introduced an expression vector according to claim 58;  
whereby said cell expresses said polypeptide encoded by said polynucleotide molecule; and  
recovering said expressed polypeptide.

61. An isolated polypeptide having the sequence of SEQ ID NO:2.

62. A polypeptide of claim 61, in combination with a pharmaceutically acceptable vehicle.

# ISR INTERNATIONAL SEARCH REPORT

EP00902354

International Application No

PCT/US 00/00396

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/11 C07K14/705 A61K38/17 A61K39/395

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data, BIOSIS

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 39361 A (ST. JUDE CHILDREN'S RESEARCH HOSPITAL) 11 September 1998 (1998-09-11) cited in the application the whole document	56-63
X	G-U VON BÜLOW AND R J BRAM: "NF-AT activation induced by a CAML-interacting member of the tumor necrosis factor receptor superfamily" SCIENCE., vol. 278, 3 October 1997 (1997-10-03), pages 138-141, XP002140938 AAAS. LANCASTER, PA., US cited in the application the whole document	56-63

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

23 June 2000

Date of mailing of the international search report

07/07/2000

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21/09/2000

# ISR INTERNATIONAL SEARCH REPORT

EP00902354

International Application No

PCT/US 00/00396

**C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT**

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 98 18921 A (HUMAN GENOME SCIENCES) 7 May 1998 (1998-05-07) cited in the application the whole document ----	1-63
A	EP 0 869 180 A (SMITH KLINE BEECHAM CORPORATION) 7 October 1998 (1998-10-07) the whole document ----	1-63
T	J A GROSS ET AL.: "TACI and BCMA are receptors for a TNF homologue implicated in B-cell autoimmune disease" NATURE., vol. 404, 27 April 2000 (2000-04-27), pages 995-999, XP002140939 MACMILLAN JOURNALS LTD. LONDON., GB ISSN: 0028-0836 the whole document -----	1-63



# INTERNATIONAL SEARCH REPORT

EP00902354

Information on patent family members

International Application No

PCT/US 00/00396

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9839361 A	11-09-1998	US 5969102 A AU 6685498 A EP 0964874 A	19-10-1999 22-09-1998 22-12-1999
WO 9818921 A	07-05-1998	AU 7674596 A BR 9612752 A EP 0939804 A	22-05-1998 18-01-2000 08-09-1999
EP 869180 A	07-10-1998	CA 2232743 A JP 10323194 A JP 2000060580 A	02-10-1998 08-12-1998 29-02-2000